Remarks

I. Status of claims

Claims 4, 6-7 and 18-19 are pending in this application. Applicants acknowledge that the rejections made under 35 U.S.C. §§ 102 and 103 in the Office Action dated July 29, 2002, have been withdrawn.

The current Office Action Summary states that the claims are subject to a restriction or election requirement. The Detailed Action, however, does not appear to contain such a requirement. Applicants have therefore not made any election.

II. Rejections under 35 U.S.C. § 112

Claims 4, 6-7 and 18-19 were rejected under 35 U.S.C. § 112, first paragraph, for failing to enable "preventing" congestive heart failure. The Examiner mentioned that one of ordinary skill in the art would not know how to totally prevent the occurrence of congestive heart failure and that the examples do not demonstrate the absolute prevention of congestive heart failure. The Examiner did mention that the substitution of "reducing the risk of onset/occurrence" in claim 4 may overcome the rejection. Applicants have amended claim 4 to recite a method for reducing the risk of onset of congestive heart failure. The specification at page 11, lines 12-14, supports this amendment. That portion of the specification notes that "[t]he number of patients who developed CHF was significantly reduced by 21% in the ramipril group, which is unexpected since patients had no signs or symptoms of CHF at study start." Applicants therefore respectfully request that the Examiner withdraw this rejection.

Claims 4, 6-7 and 18-19 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the use of the phrase "essentially maintained heart function." The Examiner questioned whether a hypertensive or hypotensive patient has essentially maintained heart function or whether a patient afflicted with hyperlipidemia has essentially maintained heart function. Applicants respectfully traverse this rejection.

Those skilled in the art understand that an "essentially maintained heart function" is determined with reference to the left ventricular ejection fraction of the patient. A person having left ventricular dysfunction would not have an essentially maintained heart function. For example, and as noted by applicants in the Amendment filed on

January 27, 2003, an ejection fraction of $\leq 35\%$ reflects left ventricular dysfunction and thus a heart function that is not essentially maintained. Whether a patient is hypertensive or hypotensive or has hyperlipidemia, as posed by the Examiner, is not determinative. In view of this explanation, applicants respectfully request that the Examiner withdraw this rejection.

III. Rejections under 35 U.S.C. § 103(a)

Claim 4 was rejected under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 4,587,258 to Gold et al. ("Gold") in view of The Merck Manual. In support of the rejection, the Examiner stated that Gold discloses a method for treating hypertension and congestive heart failure ("CHF") through the administration of ACE inhibitors. The Examiner then referred to The Merck Manual as disclosing that hypertension is one of the causes of CHF. The Examiner concluded that it would have been obvious to combine the two disclosures to employ an ACE inhibitor in a method of controlling or treating hypertension, an underlying cause of CHF, thereby preventing the onset of CHF. Applicants respectfully traverse this rejection.

Those skilled in the art understood that the treatment of hypertension itself would not necessarily reduce the risk of the onset of CHF. Other factors, for instance acute myocardial infarction, can also cause CHF. Knowing that factors other than hypertension can cause CHF, the treatment of hypertension would not have given one skilled in the art a reasonable expectation of success in reducing the risk of onset of CHF.

The comments provided by the applicants in the Amendment dated January 27, 2003, illustrate that the rational for the rejection is not as straightforward as it may seem. The art reflected a belief that angiotensin converting enzyme inhibitors brought about their beneficial effects through their action on functionally impaired cardiac muscle. A patient having essentially maintained heart function would not suffer from such impairment of the cardiac muscle. Absent that condition, there would not have been a reasonable expectation of success in preventing congestive heart failure in that patient. To support these arguments, applicants cited commentary on the SOLVD and SAVE Trials that cautioned against extrapolating the results of the trials to patients

having ejection fractions above 0.35 (SOLVD) or above 0.40 (SAVE). Those doubts remained even though angiotensin converting enzyme inhibitors were already known to be useful for the treatment of hypertension. The documents cited by the applicants provide persuasive evidence that the connection between the treatment of hypertension and the prevention of CHF was too weak to conclude that the former provided a reasonable expectation of success in doing the latter. For at least these reasons, applicants respectfully request that the Examiner withdraw the rejection of claim 4.

Claims 6-7 and 19 were rejected under 35 U.S.C. § 103(a) as unpatentable over Gold and The Merck Manual as explained above and further in view of WO 96/24373. Applicants respectfully traverse this rejection. Claims 6-7 and 19 should be patentable in view of Gold and The Merck Manual for the same reasons explained for claim 4. The Examiner relied on WO 96/24373 for a teaching of specific angiotensin converting inhibitors. That teaching, even if combined with the primary references, would not render claim 4 obvious and therefore would not render claims 6-7 or 19 obvious either. Applicants therefore respectfully request that the Examiner withdraw this rejection.

IV. Rejection under 35 U.S.C. § 102

Claims 4 and 18 were rejected under 35 U.S.C. § 102(b) as unpatentable in view of an Abstract of Allen et al., "Diabetic Vascular Hypertrophy and Albuminuria: Effect of Angiotensin Converting Enzyme Inhibition," J. Diabetes Complications, vol. 9, pp. 318-322 (1995). Applicants enclose a copy of the full Allen et al. document in the accompanying Supplemental Information Disclosure Statement and respectfully traverse this rejection.

Allen discloses a study of the role of angiotensin converting enzyme inhibition with ramipril on mesenteric vascular hypertophy and urinary albumin excretion in a normotensive model of experimental diabetes. The authors conclude that ramipril will attenuate the development of mesenteric vascular hypertophy after 24 weeks of experimental diabetes. *See* Allen at page 319, under "Discussion." The document does not disclose the prevention of CHF and does not even appear to discuss the details of any effects of ramipril on cardiac function generally. For at least these reasons, the document does not teach or suggest the subject matter of claims 4 and 18.

If the Examiner decides to maintain this rejection, applicants respectfully request that the Examiner identify where the Allen et al. document is believed to teach the claimed invention.

In light of the above, the pending claims should be in condition for allowance. If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: October 9, 2003

By: _____
Steven J. Scott
Reg. No. 43,911

Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claim in the application and Applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
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Dated: October 9, 2003

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